

### Remarks/Arguments

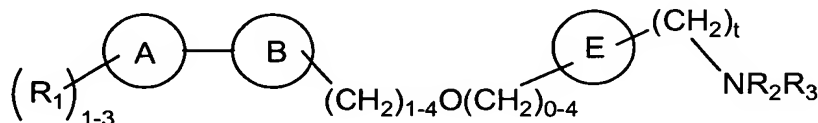
Claims 1-17 are pending in this application. Claims 1-13 are rejected. Claims 14-17 are withdrawn from consideration.

Claim 1 has been amended by limiting the definition of B to thiazole and the definition of A and E to phenylene. Claims 2 and 3 have been canceled.

Applicant's invention relates to a series of substituted heteroaryl and heterocyclic compounds, pharmaceutical compositions and methods for the use thereof in treating or ameliorating an inflammatory disorder.

As a result of the restriction requirement applicant elected the subject matter of Group I, i.e. claims 1-13, which are drawn to the products of Formula (1).

Pursuant to Applicant's election of compound No. 3 of Formula(1a) as the species for further examination, the scope of the invention was limited by the Examiner to the following substitutions of the base structure:



wherein:

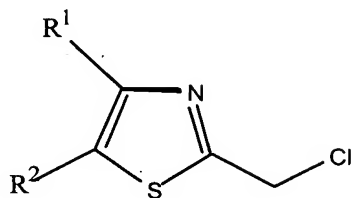
$R_1$  represents halogen with one substitution in the 3, 4 and 5 positions;  
A represents phenylene;  
B represents thiazole;  
the linker between A and E represents  $-CH_2O-$ ;  
E represents phenylene;  
 $t$  equals 1;  
 $R_2$  represents hydrogen; and  
 $R_3$  is as defined.

As a result of the election and the scope of the invention as defined above, the remaining subject matter of claims 1-12 is withdrawn from further consideration.

Claims 1-12 are objected to for containing elected and non-elected subject matter. By the present amendment the claims have been amended so as to remove the non-elected subject matter as defined by the Examiner at the bottom of page 2 of the office action.

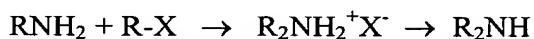
Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lau *et al.* (Bioorganic & Medicinal Chemistry Letters, 1995, 1615-1620) in view of McMurry (Organic Chemistry, 4th Edition pp 377-385, 603-604, 679-680 and 946-947) and Dominianni *et al.* (WO 96/13264).

The Examiner has pointed out that Lau *et al.* teach a thiazole of the formula:

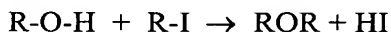


wherein R<sup>1</sup> is 4-Cl-phenyl and R<sup>2</sup> is H (compound 11 on page 1617). The Examiner concedes, however, that Lau *et al.* do not teach applicant's claimed compound.

McMurry is a basic text book on Organic Chemistry. The Examiner states that McMurry on pages 603-604 teaches the bromination of alkylbenzene side chains using N-bromosuccinimide. The Examiner then states that McMurry teaches the substitution of halogen by ammonia via an S<sub>N</sub>2 reaction on pages 377-385. The Examiner appears to be referring to the reaction on page 384 wherein the alkyl halide CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>Br is reacted with N<sub>3</sub><sup>-</sup> to form CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>N<sub>3</sub> + Br<sup>-</sup>. The Examiner states further that McMurry teaches the process for alkylation of a primary amine by an alkyl halide and refers to pages 946-947. The pages cited by the Examiner illustrate the reaction of a primary amine with an alkyl halide to form a secondary amine :



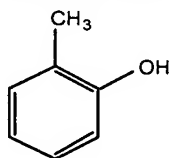
Having cited several isolated reactions in the text, the Examiner then states that McMurry teaches the formation of an ether linkage via the Williamson ether synthesis on pages 679-680. The reaction is essentially that of an alcohol with an alkyl halide to form an ether:



The Examiner then concludes that it would be obvious for one of ordinary skill in the art to brominate ortho-, meta- or para-cresol with N-bromosuccinimide, react the product formed with ammonia to yield a primary amine, alkylate said primary amine with any alkyl halide and react the resulting phenol with the thiazole compound of Lau *et al.* to create applicant's claimed compound with a reasonable expectation of success. It is submitted that the reaction scheme set forth by the Examiner is pure speculation. There is nothing in any of the references cited by the Examiner which would indicate that applicant's claimed compounds could be prepared via the various steps proposed by the Examiner.

To begin with, applicant is not claiming a process for making the claimed compounds. As indicated above applicant's invention relates to a series of substituted heteroaryl and heterocyclic compounds useful in treating inflammatory disorders.

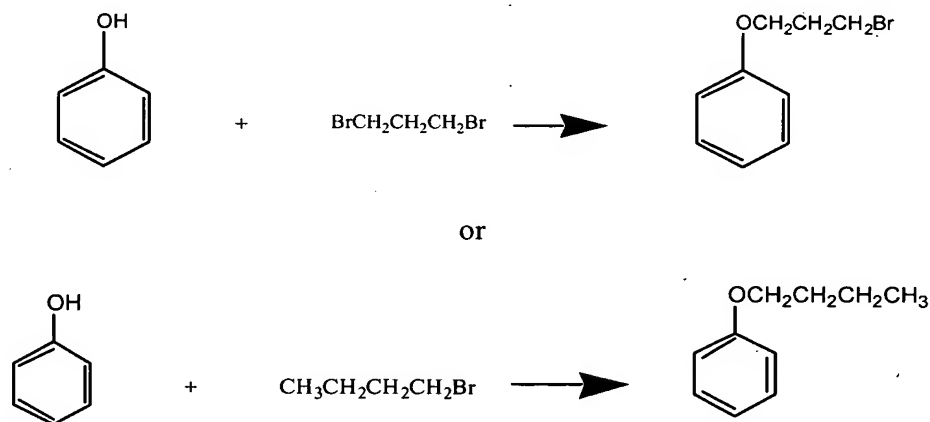
The reaction with N-bromosuccinimide in McMurry referred to by the Examiner is carried out with an alkyl benzene. Cresols are not alkyl benzene compounds but rather alkyl phenols. For example, o-cresol has the following formula:



There is nothing in the passage in McMurry to indicate that the cited bromination of an alkyl benzene compound will proceed equally as well with an alkyl phenol.

Ammonia is known to react with alkyl halides to yield a primary alkyl amine. There is nothing in McMurry to indicate that the reaction a haloalkyl phenol with ammonia will result in an amino alkyl phenol.

Alkyl phenyl ethers are prepared from Phenols by the Williamson synthesis referred to above. The  $S_N2$  reaction of a phenol with an alkyl halide proceeds as follows:



[See: Introduction to Organic Chemistry, 2nd Ed., Streitweisser *et al.* 1981,1999]

The Examiner proposes to react an amino alkyl phenol with an alkyl halide to form an alkylated amino phenol. However, as pointed out above, phenols react with alkyl halides to form alkyl phenyl ethers. The product of the reaction of an amino alkyl phenol with an alkyl halide, therefore, would be an alkyl phenyl ether. In the last step of the synthesis proposed by the Examiner a phenol is reacted with the chloro alkyl thiazole of Lau to form applicant's claimed compound. However, there is nothing in either Lau *et al.* or in McMurry to indicate that a chlorophenyl substituted chloro alkyl thiazole will

react with an alkylated amino phenol to form an ether. Chloro alkyl thiazoles are not typical alkyl halides. However, since the previous step in the synthesis results in an alkyl phenyl ether, there would be no phenol to react with the thiazole compound.

It is submitted that the Examiner has merely cited several unrelated reactions from a text book and an unrelated publication and concluded that it would be obvious to use these reactions to prepare applicant's compounds, in spite of the fact that nothing resembling applicant's compounds is disclosed in either Lau *et al.* or McMurry.

The Examiner states that the motivation to prepare the claimed compounds is provided by Dominanni *et al.* who teach a process for preparing structurally similar compounds. The Examiner cites page 2, lines 10-18 and page 50, Part B of Example 18 in the reference. The compound prepared in Example 18 of the reference is an intermediate in the preparation of the C-substituted pentacycloazoles and N-alkyl substituted pentacycloazoles which are the subject of the cited application. The passage on page 2 of the reference relates to the final pentacycloazole compounds and not, as suggested by the Examiner, to the intermediate compound prepared in Example 18. The compound prepared in the reference contains an oxazole ring while applicants compounds contain a thiazole ring. In addition the reference compound has a primary amine attached to the alkoxy phenyl ring. It should be noted that the amine prepared by Dominanni *et al.* in Example 18 is prepared by first preparing a benzonitrile derivative which is then reduced to an amine with lithium aluminum hydride. Applicant's compounds are prepared via a multi-step process which is illustrated on pages 12-15 of the specification and bears no resemblance to the synthesis proposed by the Examiner.

Applicant is not claiming a process for preparing the claimed heterocyclic compounds. There is nothing in McMurry or Lau *et al.* which would indicate that the claimed phenyl thiazole alkoxybenzene alkyamino compounds could be prepared by the isolated steps proposed by the Examiner. As indicated above the compounds prepared by Dominanni *et al.* are oxazolyl derivatives which are intermediates in the preparation of the N-alkyl-substituted pentacycloazoles. No utility for the intermediates is referred to in the application. It is submitted that no combination of the references cited by the Examiner renders applicant's claimed compounds *prima facie* obvious.

Although applicant has elected the species set forth on page 2 of the office action, applicant submits that the election was solely for the purpose of examination. Since it is applicants position that the claimed compounds are not obvious over the references cited by the Examiner, it is believed that applicant is entitled to the reasonable definitions of t, R<sub>1</sub> and R<sub>2</sub> set forth in the claims as filed. Therefore, in amending the claims, applicant has only limited the definition of A, B and E to conform to the restriction requirement.

In view of the above discussion and the amendments herein being made to the claims, it is believed that all of the outstanding objections and rejections have been removed. Reconsideration of the rejection of claims 1-13 under 35 U.S.C. 103(a) is courteously requested.

Docket No. PRD0017USNP  
Serial No. 10/612,187

Applicants respectfully request that a timely Notice of Allowance be issued in this application.

Respectfully submitted

By: /John W. Harbour/  
John W. Harbour  
Reg. No. 31,365  
Attorney for Applicants

Johnson & Johnson  
One Johnson & Johnson Plaza  
New Brunswick, NJ 08933-7003  
(732) 524-2169  
Dated: April 27, 2006